ReFORMÚLaTE

TOP 10
"DE BARCELONA NO TE IRÁS SIN SABER 10 COSAS MÁS"

@Farmacia_LaPaz

@67CongresoSEFH

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Y más novedades farmacoterapéuticas 2021-2022…

6. Terapia génica in vivo
7. Nuevo algoritmo de tratamiento del *Clostridioides difficile*
8. Terapia no sustitutiva en hemofilia
9. Novedades en el abordaje de la diabetes en enfermedad renal crónica
10. Novedades en vacunas (no COVID)

Top 6 - Terapia génica in vivo

Es una terapia avanzada

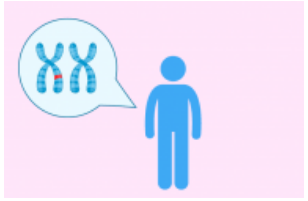
Terapias avanzadas : medicamentos con procesos de fabricación basados en moléculas biológicas producidas por transferencia genética y/o en células terapéuticas modificadas biológicamente como sustancias activas o parte de las mismas.

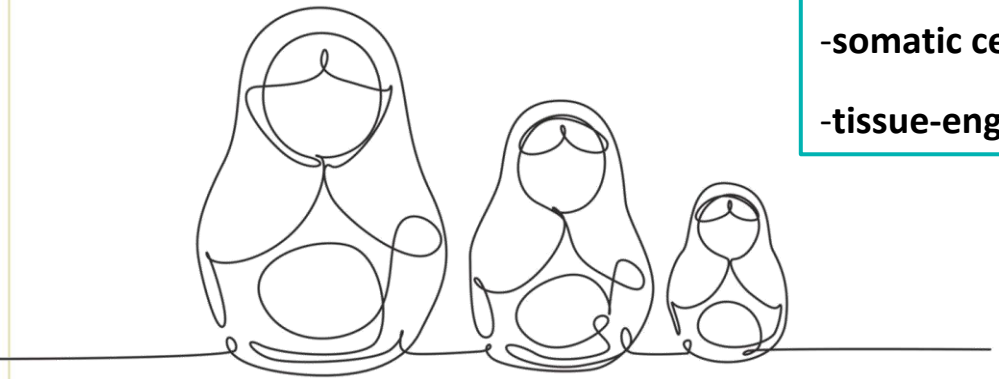
Advanced therapy medicinal products (ATMPs) include:

-**gene therapy** medicinal products,

-**somatic cell therapy** medicinal products

-**tissue-engineered pr**





Terapia génica: inserting 'recombinant' genes into the body that lead to a therapeutic, prophylactic or diagnostic effect, to treat a variety of diseases, including genetic disorders, cancer or long-term diseases.

Real Decreto 1345/2007, por el que se regula autorización, registro y condiciones de dispensación de los medicamentos de uso humar
EUR-Lex: Directive 2001/83/EC of the European Parliament on the Community code relating to medicinal products for human use

Transducción de exogen transgénico en células vivas.

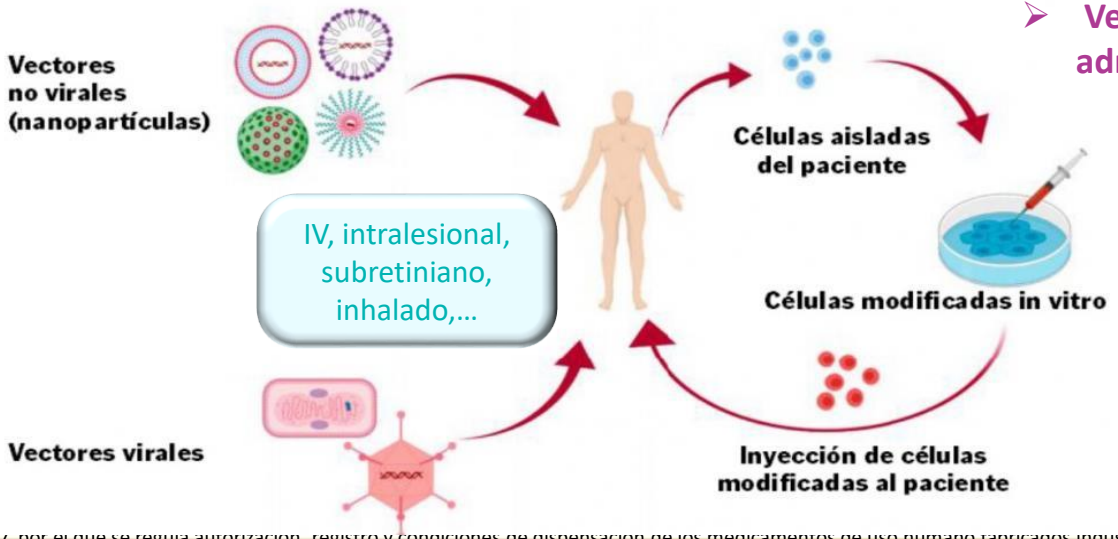
VECTOR

Terapias génicas según "principio activo":

- **Células alo/xenogénicas a las que se les transfiere vector con transgen.**
- **Vector preparado para transferir a células autólogas y reintroducir en organismo**
- **Vector con transgen preparado para su administración directa.**

Terapia génica in vivo

Terapia génica ex vivo

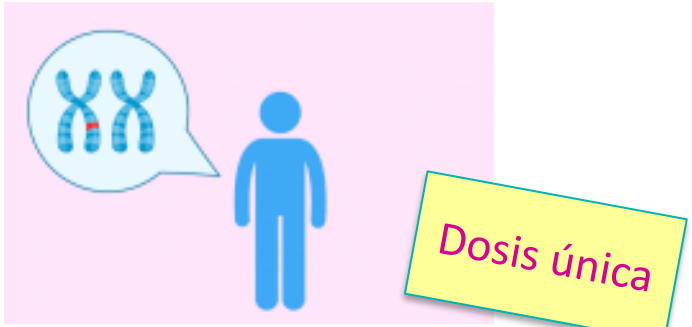


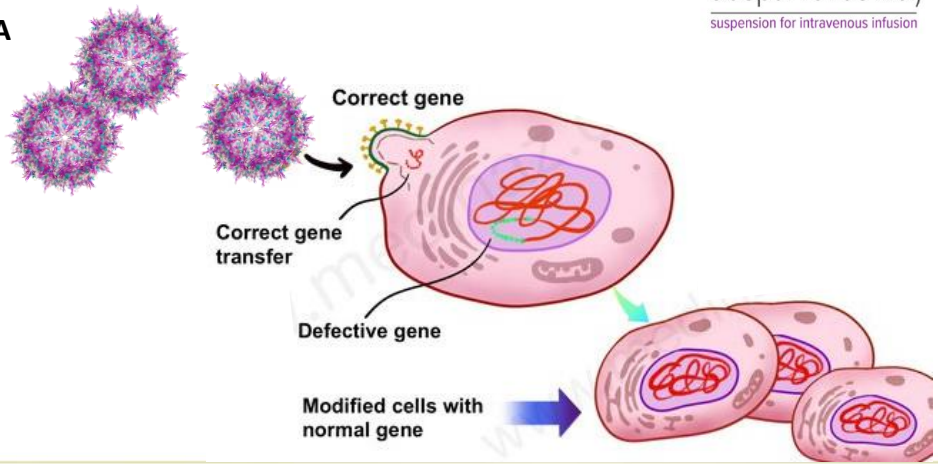
Real Decreto 1345/2007, por el que se regula autorización, registro y condiciones de dispensación de los medicamentos de uso humano fabricados industrialmente.

Primeros medicamentos de terapia génica in vivo comercializados 2021-2022

MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios

- **Voretigén neparvovec**: indicado en amaurosis congénita de Leber (LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection)
- **Onasemnogén abeparvovec**: indicado en atrofia muscular espinal (AME) (zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion)





LUXTURNA™
voretigene neparvovec-rzyl
for subretinal injection

Voretigén neparvovec

Amaurosis congénita de Leber.

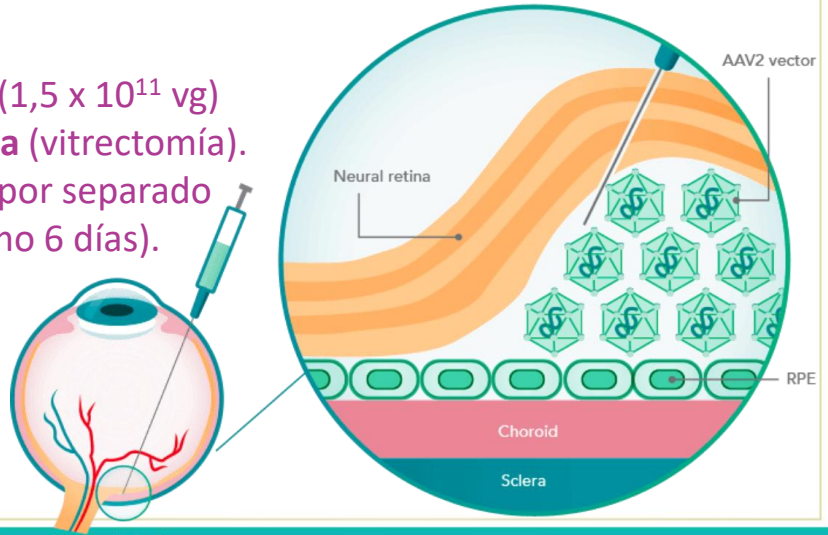
Distrofia retiniana degenerativa asociada a mutación RPE65 bialélica.

Primera causa de ceguera congénita severa

Principio activo compuesto de:

- ✓ producto transgénico: **ADN complementario** de proteína de 65 kDa del epitelio pigmentario retinal humano [**RPE65**].
- ✓ vector viral adeno-asociado 2 (**AAV2**).

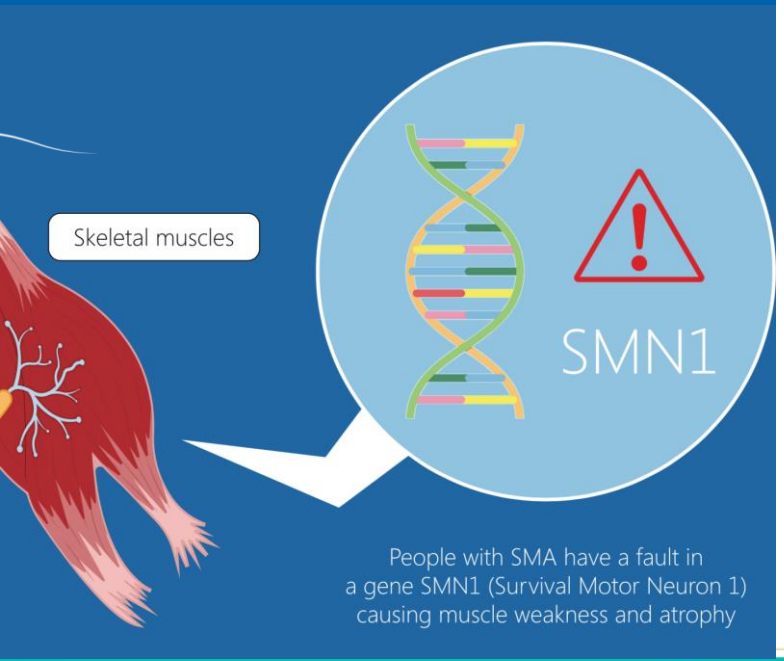
Dosis **fija** (1,5 x 10^{11} vg) **subretiniana** (vitrectomía). Cada ojo por separado (mínimo 6 días).



zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

Onasemnogén abeparvovec

Atrofia muscular espinal (AME) con mutación bialélica SMN1.



Atrofia muscular temprana con pérdida de tono, deglución y ventilación.

Principio activo compuesto de:

- ✓ producto transgénico: ADN funcional de **gen SMN1**.
- ✓ vector viral adeno-asociado 9 (**AAV9**). BHE

- Dosificación **por peso** ($1{,}1x10^{14}$vg/kg). Administración **IV** perfusión 60'.
- **Toxicidad**: ↑TSM, ↑troponina I y trombocitopenia. Riesgo MAT. **Controles periódicos**.

Limitaciones y retos TG in vivo

- Test Ac antivirales
- Corticoides para **inmunosupresión**
- Contraindicado en infecciones activas
- **Riesgo biológico**:
  - ❖ Protección personal manipulador
  - ❖ Gestión de residuos del paciente.
- **Seguridad a largo plazo**
- ¿Monoterapias de **dosis única**?
- Costes

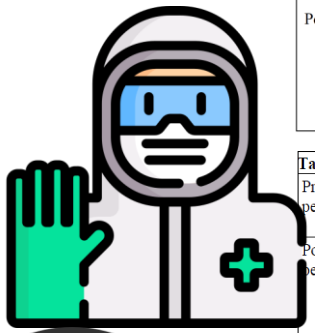


Tabla 1 **Pauta inmunomoduladora pre y postoperatoria para cada ojo**

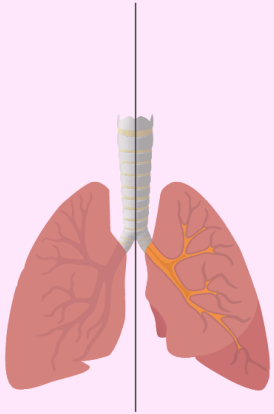
Preoperatorio	3 días antes de la administración de Luxturna	Prednisona (o equivalente) 1 mg/kg/día (hasta un máximo de 40 mg/día)
Postoperatorio	4 días (incluyendo el día de la administración)	Prednisona (o equivalente) 1 mg/kg/día (hasta un máximo de 40 mg/día)
	Continuar 5 días	Prednisona (o equivalente) 0,5 mg/kg/día (hasta un máximo de 20 mg/día)
	Continuar 5 días con una dosis cada dos días	Prednisona (o equivalente) 0,5 mg/kg cada dos días (hasta un máximo de 20 mg/día)

Tabla 2 **Régimen inmunomodulador previo y posterior a la perfusión**

Previo a la perfusión	24 horas antes de la administración de onasemnogén abeparvovec	Prednisolona por vía oral 1 mg/kg/día (o equivalente si se utiliza otro corticosteroide)
Posterior a la perfusión	30 días (incluido el día de la administración de onasemnogén abeparvovec)	Prednisolona por vía oral 1 mg/kg/día (o equivalente si se utiliza otro corticosteroide)
	Seguido de 28 días:	Los corticosteroides sistémicos deben reducirse gradualmente.

Futuro próximo en TG in vivo

β-talasemia



Fibrosis quística

Distrofias musculares de Duchenne y Becker

Hemofilia

Top 7 - Nuevo algoritmo de tratamiento del *Clostridioides difficile*

Clinical Microbiology and Infection 27 (2021) S1–S21

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults

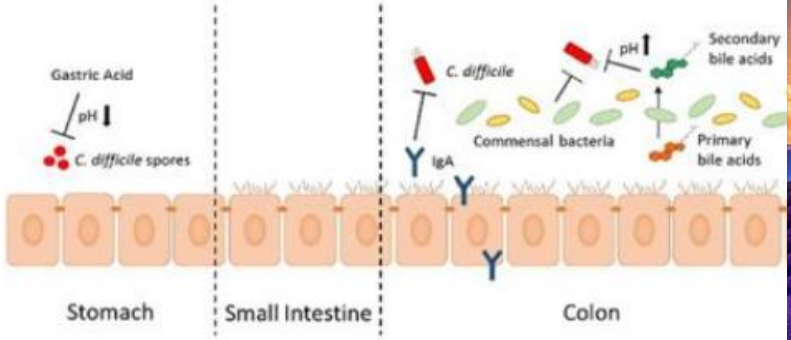
Processes Leading From Asymptomatic *C. difficile* Colonization to CDI

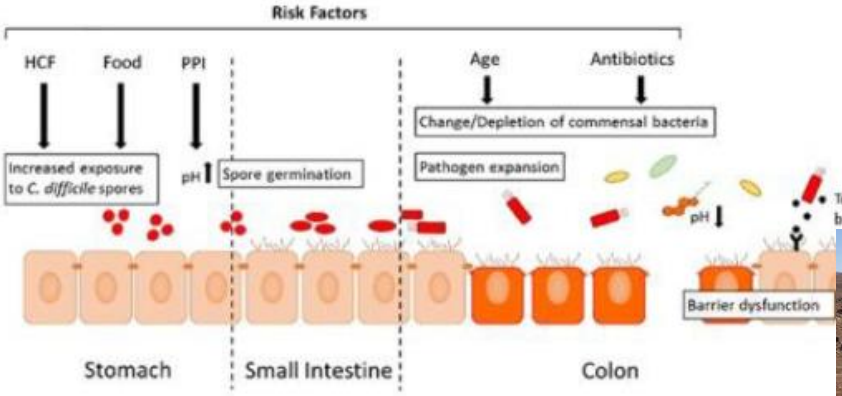
ReFORMULaTE

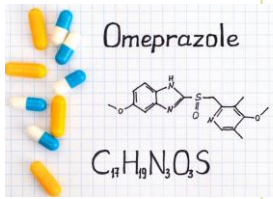
Asymptomatic colonization

Factors controlling *C. difficile*
- Colonization resistance
- Bacteriocin secretion
- Bile acids composition
- Increased IgA levels

C. difficile infection (CDI)

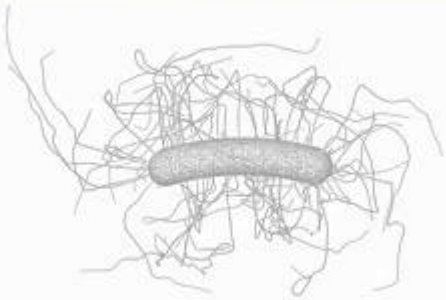






Abbreviations: CDI, C. difficile infection; HCF, health care facilities; IgA, Immunoglobulin A; PPI, proton pump inhibitor; TcdA, C. difficiletoxin A; TcdB, C. difficile toxin B.

Front Microbiol. 2018 Apr 10;9:64



Infección por *Clostridiodes difficile* (ICD)

Diarrea no complicada (≥3 depo/24h) >>> megacolon tóxico / perforación / sepsis.

Gravedad

Recurrencia

including CDI recurrence, associated with hospital readmissions.

Results: The study included 3,950 patients with CDI from 2003-2009, including 413 patients with recurrent CDI. Recurrent CDI patients were significantly more likely to have at least 1 readmission (85% vs 41%; $P < .001$) and had more days readmitted (mean = 18.6 vs 7.6; $P < .001$) than patients without recurrent CDI. In multivariable analysis, recurrent CDI was independently associated with number of readmissions (rate ratio = 2.54; 95% confidence interval [CI], 2.21-2.91) and days readmitted (rate ratio = 3.97; 95% CI, 3.11-5.08) after adjustment for demographics, comorbidities, and medications. ***Conclusion:*** Recurrent CDI patients are significantly more likely than patients without a recurrence to be readmitted and spend increased time readmitted to the hospital.

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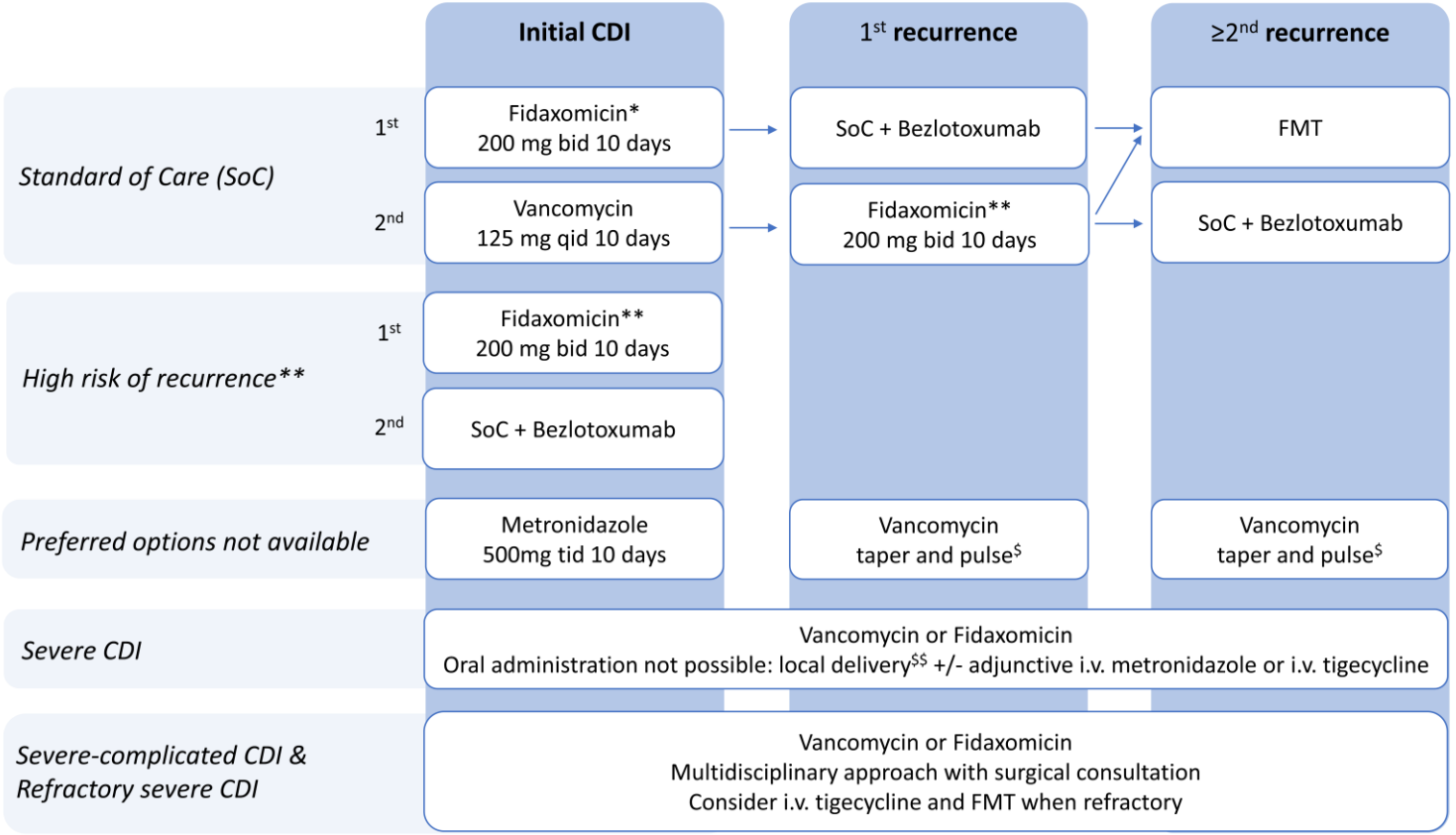
VII. **Can prognostic factors identify patients at risk for severe CDI?**

- The most important risk factors for severe CDI are older age (>65 years old) and presence of multiple comorbidities. *Strong, Moderate*

VIII. **Can prognostic factors identify patients at risk for recurrent CDI?**

- Older age (>65 years old) is the most important risk factor for recurrent CDI. *Strong, Moderate*
- Patients with prior CDI episode(s) are at an increased risk for recurrent CDI. *Strong, Moderate*
- Patients with healthcare-associated CDI and prior hospitalization in the last three months are considered at increased risk for recurrent CDI. *Weak, Low*
- Patients with concomitant non-CDI antibiotic use after the diagnosis of CDI are considered at increased risk for recurrence of CDI. *Weak, Very low*
- Patients using PPIs started during/after CDI diagnosis are considered at increased risk for recurrent CDI. *Weak, Very low*



* Risk stratification for risk of recurrence may be applied for selective use of fidaxomicin in case of limited access or resources.

** Consider extended fidaxomicin: 200 mg bid on day 1-5, 200 mg q48h on day 7-25. Most important risk factor for recurrence is age >65-70 years. Additional risk factor(s) to consider are healthcare-associated CDI, prior hospitalization ≤ 3 months, prior CDI episode, continued non-CDI antibiotic use, and PPI therapy started during/after CDI diagnosis. The risk of recurrence is assumed higher with more risk factors present.

$ Vancomycin taper and pulse: 2 weeks 125 mg qid, followed by 1 week 125 mg bid, then 1 week 125 mg qd, then 1 week 125 mg q48h, and finally 125 mg q72h for 1 week.

$$ Rectal or nasoduodenal delivery

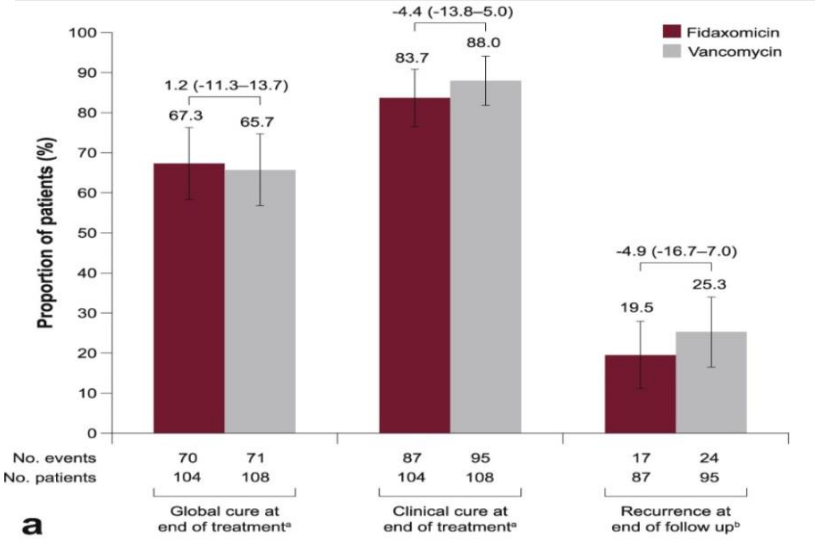
Fig. 1. Suggested treatment algorithm.

- Discontinuation of unnecessary antimicrobial therapy
- Adequate replacement of fluid and electrolytes
- Avoidance of anti-motility medications
- Reviewing proton pump inhibitor (PPI) use.

Antibióticos

- ✓ Suspensión de antibióticos
- ✓ Adecuar tratamiento para CD

¿Cuál es el mejor tratamiento inicial?



Louie et al. N Engl J Med 2011;364:422-31

¿Cuál es el mejor tratamiento inicial?

Vancomicina vs fidaxomicina

- Igual % curación
- Fidaxomicina menos recurrencia

Initial CDI		
Standard of Care (SoC)	1st	Fidaxomicin* 200 mg bid 10 days
	2nd	Vancomycin 125 mg qid 10 days
*High risk of recurrence***	1st	Fidaxomicin** 200 mg bid 10 days
	2nd	SoC + Bezlotoxumab

VALORAR RIESGO DE RECIDIVA

Ya NO recomendado METRONIDAZOL

Excepto uso IV en intolerancia oral/íleo paralítico.

Alternativa en casos leves en at. primaria (500mg /8h VO x10d)

No recomendado

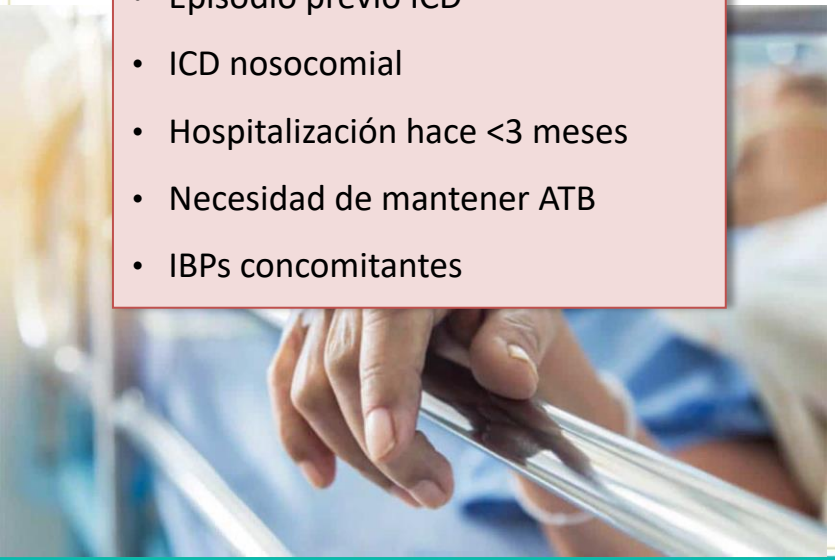
vancomicina 500mg c/6h VO

TRATAMIENTO PRIMER EPISODIO

CON ALTO RIESGO DE RECIDIVA

Grupos de mayor riesgo de recidiva:

- **≥ 65 años***
- Episodio previo ICD
- ICD nosocomial
- Hospitalización hace <3 meses
- Necesidad de mantener ATB
- IBPs concomitantes



*High risk of recurrence***	1st	Fidaxomicin** 200 mg bid 10 days
	2nd	SoC + Bezlotoxumab

Opción 1: **Fidaxomicina 200 mg /12 h** VO 10 días

Opción 2: **Vancomicina 125 mg /6h** VO 10 días

+

Bezlotoxumab 10mg/kg IV (Mab antirrecidiva) dosis única durante el episodio

V. **What is the best treatment for recurrent CDI?**

- If the initial CDI episode was treated with vancomycin or metronidazole, then fidaxomicin 200 mg twice daily for 10 days is the preferred agent to treat a first CDI recurrence. *Strong, Low*
- If the initial CDI episode was treated with fidaxomicin, consider addition of bezlotoxumab (when available and feasible) to an oral SoC antibiotic treatment, i.e. vancomycin or fidaxomicin. *Addition to vancomycin: omicin: good practice state*
- Consider a vancomycin tap CDI when fidaxomicin or feasible. *Weak, Very low*

¿Cómo tratamos la recurrencia de ICD?

TRATAMIENTO EN RECURRENCIA ICD

Si **NO** se usó Vancomicina	Si se usó Vancomicina
Vancomicina 125 mg / 6h VO 10 días + Bezlotoxumab 10mg/kg IV (antirrecidiva)	Fidaxomicina 200 mg/12 h VO 10 días

****Alternativa:** pulso prolongado de vancomicina (*tapering*)

- 125 mg / 6 h VO durante 14 días
- 125 mg / 12 h VO durante 7 días
- 125 mg / 24 horas VO durante 7 días
- 125 mg VO cada 3 ó 4 días durante 2 semanas más.

What is the best treatment for CDI when no oral treatment is possible?

- When oral therapy is not possible, attempt intraluminal (gastroduodenal or coloscopic) delivery of vancomycin or fidaxomicin. *Good practice statement*
- and consider adjunctive treatment with iv metronidazole 500 mg three times daily or iv tigecycline 50 mg two times daily (100 mg loading dose). *Weak, Very Low*

Therefore, when oral treatment with vancomycin or fidaxomicin is not possible, intraluminal delivery should be attempted. The evidence for intraluminal vancomycin is limited to case series and dosages range from 250 mg once daily to 1 g four times a day [211]. There are no data on intraluminal fidaxomicin delivery. It seems reasonable use standard oral dosages for intraluminal delivery.

What is the best treatment for severe or severe-complicated CDI?

after failure of another agent. Overall, there are no data that demonstrate superiority of fidaxomicin or vancomycin over the other for severe and severe-complicated CDI.

- For severe CDI, routine addition of iv metronidazole to oral SoC therapy is not recommended. *Weak, Very Low*
- When a patient is deteriorating or progressing to severe-complicated CDI while on anti-CDI antibiotic therapy, addition of iv tigecycline 50 mg twice daily (100 mg loading dose) may be considered on a case-by-case basis. *Weak, Very Low*

IX. Is there a place for prophylaxis for prevention of CDI?

- Routine administration of probiotics to prevent CDI when on antibiotic treatment is not recommended. *Strong, low*
- Routine prophylaxis with anti-CDI antibiotics when on systemic antibiotic treatment is not recommended. *Good practice statement*

- To reduce CDI we need a bundle approach with Antibiotics Stewardship
  - Hand hygiene
  - Good Isolation practice
  - Early detection and treatment
  - Environmental Cleaning
  - Education for providers, health care staff and patients

Top 8 - Terapia no sustitutiva en hemofilia

Terapia basada en reposición de factor deficitario

vs

Terapia no sustitutiva

- **AcM biespecíficos**.
- **AcM bloqueantes** de inhibidores de la coagulación.
- **ARNsi** (interferencia pequeño) que bloquean inhibidor AT-III
- **Terapia génica** in vivo.

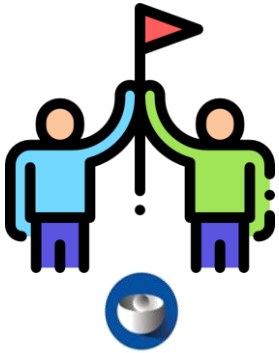
Emicizumab
Mim8

Concizumab
Marstacimab

Fitusiran

Valoctocogén roxaparvovec

Anticuerpos monoclonales biespecíficos: emicizumab



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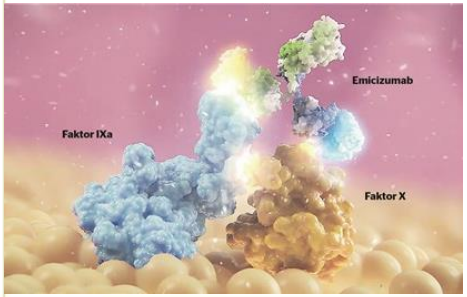
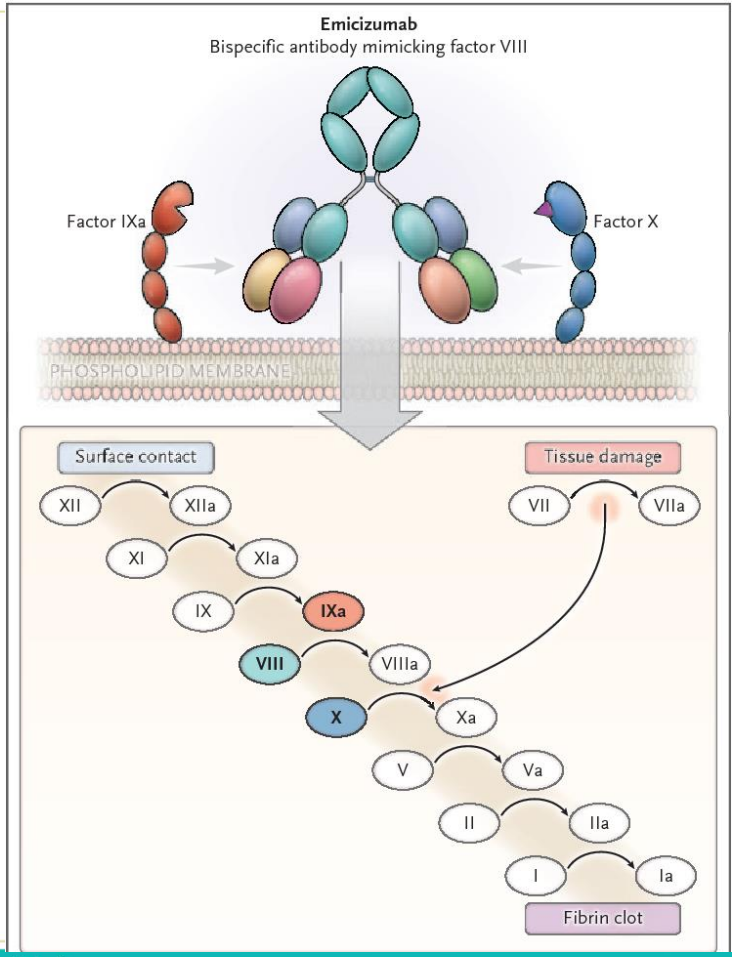
SCIENCE MEDICINES HEALTH



- Profilaxis en **hemofilia A grave**.
- AcM humanizado **mimetiza a factor VIIIa**.
- Dos puntos de unión en Fab diferentes: a FIXa y a FX
- Importantes ventajas:
  - ✓ Administración **subcutánea**
  - ✓ Gran utilidad en **pacientes con inhibidor.**



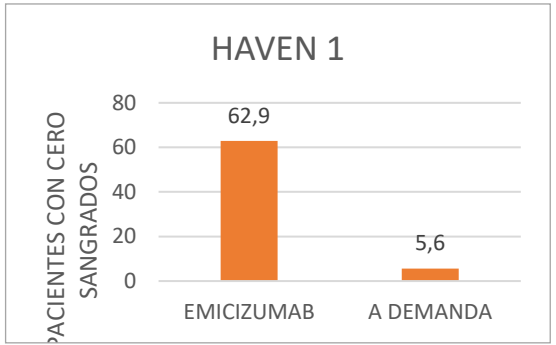
Anticuerpos monoclonales biespecíficos: emicizumab

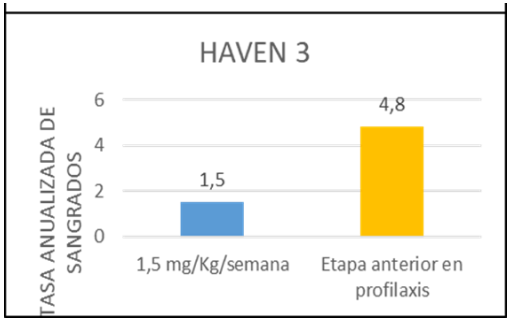
HAVEN 1	HAVEN 2	HAVEN 3	HAVEN 4
NCT02622321	NCT02795767	NCT02847637	NCT03020160
Open-label, randomized study*	Open-label, nonrandomized study	Open-label, randomized study†	Open-label, nonrandomized study
Adult/adolescent (≥12 years) PwHA **with** FVIII inhibitors N = 113	**Pediatric**§ (<12 years) PwHA **with** FVIII inhibitors N = 88	**Adult/adolescent** (≥12 years) PwHA **without** FVIII inhibitors N = 152	**Adult/adolescent** (≥12 years) PwHA **with or without** FVIII inhibitors N = 48
Emicizumab‡ 1.5 mg/kg QW	Emicizumab‡ 1.5 mg/kg QW 3.0 mg/kg Q2W 6.0 mg/kg Q4W	Emicizumab‡ 1.5 mg/kg QW 3.0 mg/kg Q2W	Emicizumab‡ 6.0 mg/kg Q4W

Con inhibidor de FVIIIa

Tabla 1. Tasa anualizada de sangrados en el estudio HAVEN1.

Tasa anualizada de sangrados (ABR) (paciente-año)	Grupo A: Profilaxis emicizumab1,5 mg/kg semanal	Grupo B: sin profilaxis
	N = 35	N = 18
Sangrados tratados ABR (IC 95%)	2,9 (1,7-5,0)	23,3 (12,3-43,9)
RR(IC 95%) p-valor	0,13 (0,06-0,28)	p < 0,0001
Todos los sangrados ABR (IC 95%)	5,5 (3,6-8,6)	28,3 (16,8-47,8)
RR(IC 95%) p-valor	0,20 (0,01-0,23)	p < 0,0001





(RR 0,32, IC 95% 0,20-0,51; p<0,0001).

Blood. 2021 Apr 22;137(16):2231-2242. doi:10.1182/blood.2020009217.

Anticuerpos monoclonales biespecíficos: emicizumab

Recommendation 5.7.1:

- For patients with hemophilia A with an inhibitor, the WFH recommends that emicizumab should be used for regular prophylaxis.
- REMARK: For patients with hemophilia A with no inhibitor, the WFH recommends that emicizumab can be used for regular prophylaxis. CB

Haemophilia. 2020;00:1–158. DOI: 10.1111/hae.14046

Indicación autorizada (MINISTERIO DE SANIDAD)	Situación expediente indicación	Resolución expediente de financiación indicación
Hemlibra está indicado para la profilaxis de rutina de los episodios de sangrado en pacientes con hemofilia A (deficiencia congénita del factor VIII) con inhibidores del factor VIII. Hemlibra puede usarse en todos los grupos de edad.	Resuelto	Sí, financiada indicación autorizada
Hemlibra está indicado para la profilaxis de rutina de los episodios de sangrado en pacientes con hemofilia A grave (deficiencia congénita del factor VIII, FVIII < 1%) sin inhibidores del factor VIII. Hemlibra puede usarse en todos los grupos de edad.	Resuelto	Sí, financiada indicación autorizada

Mejoras en calidad de vida

- ✓ Administración **subcutánea**
- ✓ **Mayor vida media**:
  - Dosis de carga: 3mg/kg x 4semanas
  - Mantenimiento: - 1,5mg/kg semanal
    - 3 mg/kg quincenal
    - 6 mg/kg mensual

Seguridad

- Aceptable: reacciones lugar de inyección (20%), cefaleas (15%) y artralgia (10%).
- Casos de **microangiopatía trombótica** grave. Asociada a CCPa >100UI/kg/24h.
- Poco inmunógeno y no genera inhibidor.

Limitación: no para tratamiento de episodios de sangrado o cirugías →**requiere suplementar con FVIII**.

Terapia génica en hemofilia: valoctocogén roxaparvovec

ROCTAVIAN

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

First gene therapy to treat severe haemophilia A Share

News 24/06/2022

AUTHORISED
This medicine is authorised for use in the European Union.

Autorización condicional

Principio activo compuesto de:

- ✓ producto transgénico: ADNc de variante SQ de **FVIII** sin dominio B.
- ✓ vector viral adeno-asociado 5 (**AAV5**).

Tropismo hepático → producción hFVIII-SQ

ROCTAVIAN está indicado para el tratamiento de la hemofilia A (deficiencia congénita de factor VIII) grave en pacientes adultos sin antecedentes de inhibidores del factor VIII y sin anticuerpos específicos contra el virus adenoasociado de serotipo 5 (AAV5) detectables.

Eficacia:

- **75%** pacientes con nivel medio **FVIII>5UI/dl** durante **2 años.**
- Reducción de ABR 85%, y reducción de suplementación 97%.

- Dosificación **por peso** ($6x10^{13}$vg/kg). Administración **IV** perfusión.
- **Toxicidad**: elevación TSM.

N Engl J Med 2022; 386:1013-1025
DOI: 10.1056/NEJMoa2113708

Top 9 - Novedades en el abordaje de la diabetes mellitus en enf. renal crónica

NUEVA GUÍA 2022

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

VOLUME 102 | ISSUE 5S | NOVEMBER 2022

www.kidney-international.org

CONSENSUS REPORT | OCTOBER 03 2022

Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO) FREE

Ian H. de Boer; Kamlesh Khunti; Tami Sadusky; Katherine R. Tuttle; Joshua J. Neumiller; Connie M. Rhee; Sylvia E. Rosas; Peter Rossing; George Bakris

Check for updates

Corresponding author: Ian H. de Boer, deboer@u.washington.edu

Diabetes Care dci220027

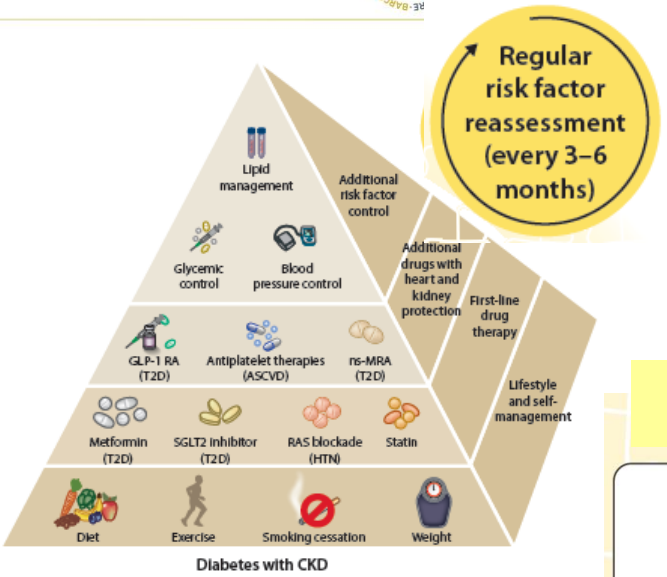
https://doi.org/10.2337/dci22-0027 **Article history**

neal dialysis. CKD is defined as persistently elevated urine albumin excretion (≥30 mg/g [≥3 mg/mmol]), persistently reduced eGFR (<60 ml/min per 1.73 m^2), or both, for greater than 3 months, in accordance with current KDIGO guidelines.

Goals

It's not just about glucose!

1. Promote self-management and team-based integrated care
2. Use organ-protective therapies
3. Treat multiple targets (glycemia, BP, lipids, UACR, eGFR)



Medicamentos con perfil cardio y nefroprotector.

Sodium (<2 g/day) and protein intake (0.8 g/kg/day)

Recommendation 3.1.1: We suggest maintaining a protein intake of 0.8 g protein/kg (weight)/d for those with diabetes and CKD not treated with dialysis *(2C)*.

Recommendation 3.1.2: We suggest that sodium intake be <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with diabetes and CKD *(2C)*.

Pharmacologic therapies

First-line therapies

Metformin (T2D, eGFR ≥30) · SGLT2 inhibitors (T2D, eGFR ≥20) · RAS inhibitors (HTN) · Statins

Additional drugs for heart and kidney protection

GLP-1 RA (T2D) · ns-MRA (T2D) · Antiplatelet therapies (ASCVD)

Primera línea DM2 + ERC

Pharmacologic therapies

First-line therapies

Metformin (T2D, eGFR ≥30)

SGLT2 inhibitors (T2D, eGFR ≥20)

RAS inhibitors (HTN)

Statins

Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i *(1A)*.

Recommendation 4.1.1: We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with metformin *(1B)*.

Recommendation 1.2.1: We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated *(1B)*.

- A statin is recommended for all patients with T1D or T2D and CKD, moderate intensity for primary prevention of atherosclerotic cardiovascular disease (ASCVD) or high intensity for patients with known ASCVD and some patients with multiple ASCVD risk factors.

Primera línea DM2 + ERC

SGLT2i

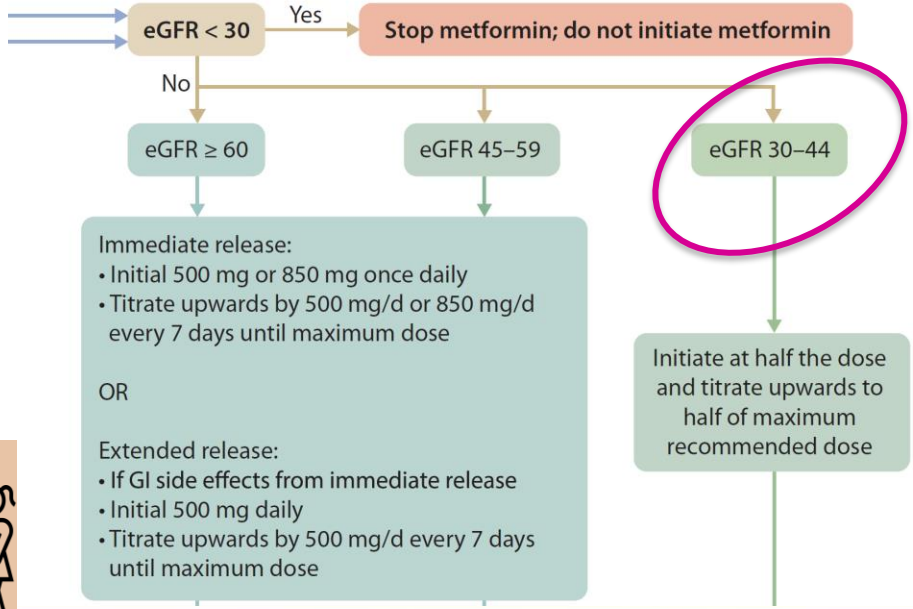
SGLT2i should be initiated for patients with T2D and CKD when eGFR is ≥20 ml/min/1.73 m² and can be continued after initiation at lower levels of eGFR. SGLT2i markedly reduce risks of CKD progression, heart failure, and atherosclerotic cardiovascular diseases, even when blood glucose is already controlled.

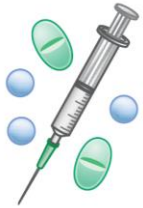
SGLT2 inhibitor	Dose
Dapagliflozin	10 mg daily
Empagliflozin	10 mg daily (Can increase to 25 mg daily if needed for glucose control)
Canagliflozin	100 mg daily (The higher dose is not recommen

Potential contraindications:
- Genital infection risk
- Diabetic ketoacidosis
- Foot ulcers
- Immunosuppression

Metformin

Metformin should be used for patients with T2D and CKD when eGFR is ≥30 ml/min/1.73 m². For such patients, metformin is a safe, effective, and inexpensive drug to control blood glucose and reduce diabetes complications.





Additional drug therapy as needed for glycemic control

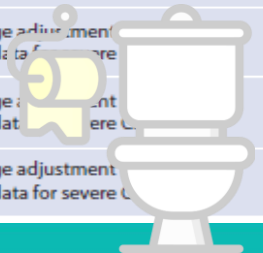
- GLP-1 receptor agonist (preferred)
- DPP-4 inhibitor
- Insulin
- Sulfonylurea
- TZD
- Alpha-glucosidase inhibitor

- Guided by patient preferences, comorbidities, eGFR, and cost
- Includes patients with eGFR < 30 ml/min per 1.73 m^2 or treated with dialysis
- See Figure 25

Recommendation 4.2.1: In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA *(1B)*.

- A glucagon-like peptide 1 (GLP-1) receptor agonist with proven cardiovascular benefit is recommended for patients with T2D and CKD who do not meet their individualized glycemic target with metformin and/or an SGLT2i or who are unable to use these drugs.

GLP-1 RA	Dose	CKD adjustment
Dulaglutide	0.75 mg and 1.5 mg once weekly	No dosage adjustment Use with eGFR >15 ml/min per 1.73 m^2
Exenatide	10 µg twice daily	Use with CrCl >30 ml/min
Exenatide extended-release	2 mg once weekly	Use with eGFR >45 ml/min per 1.73 m^2
Liraglutide	1.2 mg and 1.8 mg once daily	No dosage adjustment Limited data for severe
Semaglutide (injection)	0.5 mg and 1 mg once weekly	No dosage adjustment Limited data for severe
Semaglutide (oral)	3 mg, 7 mg, or 14 mg daily	No dosage adjustment Limited data for severe



Additional drugs for heart and kidney protection

GLP-1 RA (T2D)

ns-MRA (T2D)

Antiplatelet therapies (ASCVD)

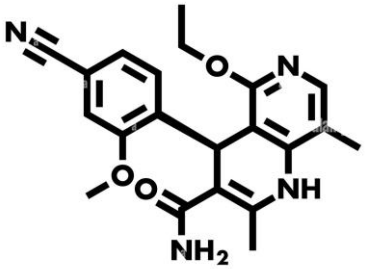
Recommendation 1.4.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for patients with T2D, an eGFR ≥25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) *(2A)*.

Practice Point 1.4.4: The choice of a nonsteroidal MRA should prioritize agents with documented kidney or cardiovascular benefits.

Currently, the only nonsteroidal MRA for which long-term clinical outcomes have been rigorously ascertained is finerenone. In the FIDELIO-DKD and FIGARO-DKD trials,

Non-steroidal mineralocorticoid antagonists (ns-MRA)

ns-MRA reduce risks of CKD progression and cardiovascular events for people with T2D and residual albuminuria. They are suggested for patients with T2D, urine ACR ≥30 mg/g, and normal serum potassium on other standard of care therapies. Serum potassium and creatinine should be monitored.



finerenone

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

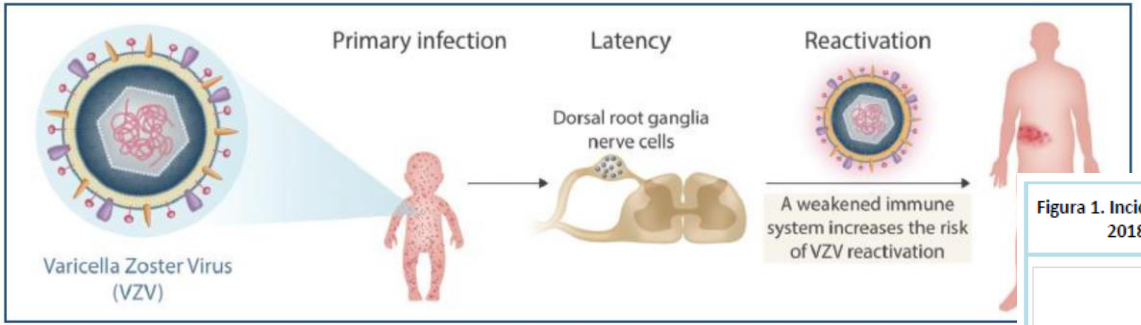
K^+ ≤4.8 mmol/l

- Initiate finerenone
  - 10 mg daily if eGFR 25–59 ml/min per 1.73 m^2
  - 20 mg daily if eGFR ≥60 ml/min per 1.73 m^2
- Monitor K^+ at 1 month after initiation and then every 4 months
- Increase dose to 20 mg daily, if on 10 mg daily
- Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l

Top 10 - **Novedades en vacunas** (no COVID)

- ✓ Nueva vacuna herpes zóster
- ✓ Avances vacuna malaria

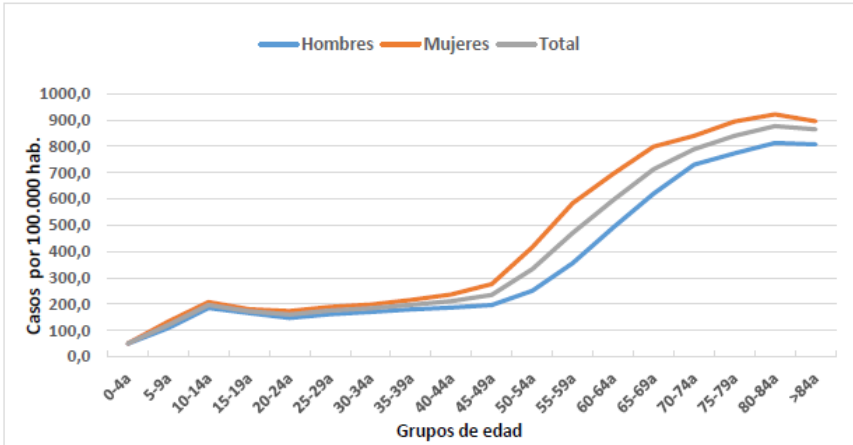
Nueva vacuna frente a Herpes zóster



Fuente: Expert Review of Vaccines, 20:9, 1065-1075

- Alta incidencia de HZ→complicaciones 30% (NPH,…)
- Incrementa con edad y condiciones de inmunosupresión.
- Implicaciones clínicas e impacto económico directos e indirectos.

Figura 1. Incidencia de herpes zóster por 100.000 habitantes, por grupo de edad y sexo. España, 2014-2018

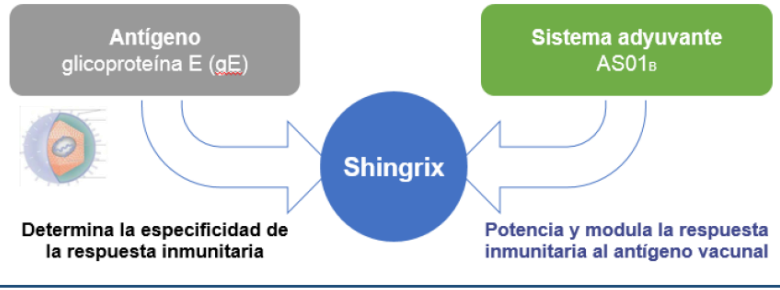


Fuentes: Red Nacional de Vigilancia Epidemiológica (RENAVE). Centro Nacional de Epidemiología. ISCIII; INE: población del Padrón municipal a 1 de enero de cada año.

Nueva vacuna frente a Herpes zóster

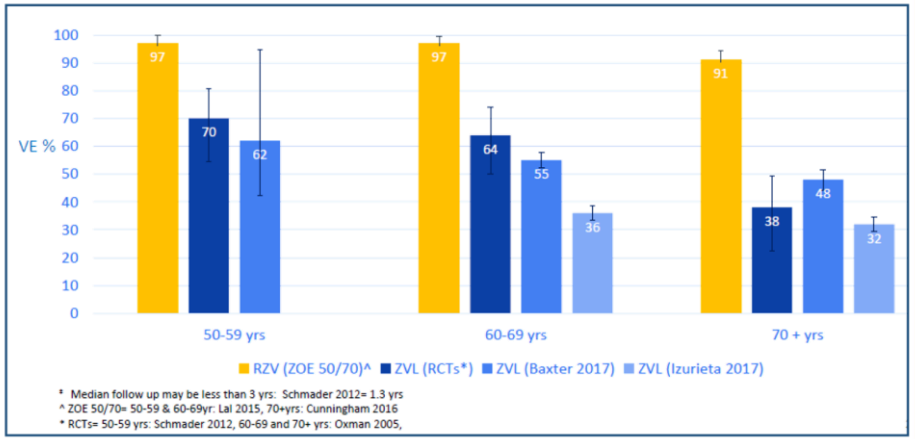
2006 aprobada vacuna VVZ atenuados (ZVL)
- ≥50 años
- Contraindicada en inmunodeprimidos
- Disminuye efectividad con edad

2022 disponible vacuna HZ adyuvada (RZV): indicada >50 años y **>18 años de grupos de riesgo**



Fuente: Dendouga et al. Vaccine 2012;30:3126–35

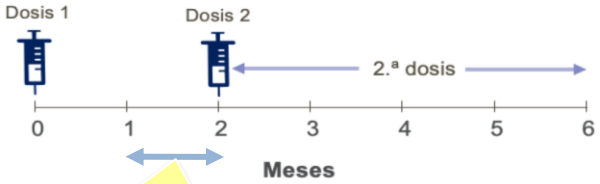
***Graf. 5** Eficacia y efectividad de RZVy ZVL frente a HZ por grupos de edad durante los primeros cuatro años después de la vacunación.*



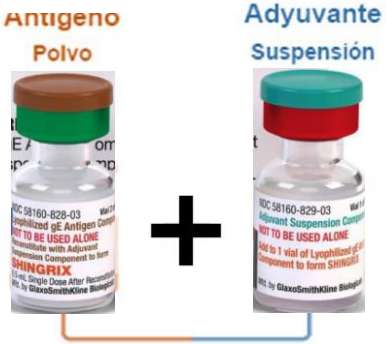
Fuente: Center for Disease Control and Prevention. Presentation by Dooling K

Nueva vacuna frente a Herpes zóster

Fuente: Dendouga et al. Vaccine 2012;30:3126–35



Inmunocomprometidos



- ✓ Vacunación en **grupos de riesgo >18 años**
- ✓ Vacunación **sistemática a los 65 años**.
- ✓ Vacunación por cohortes desde 80 años.

Compatible con vacunas gripe, VCN13, VNP23 y dTpa

Posponer si:

- fiebre
- episodio activo de HZ
- embarazo

Recomendaciones de vacunación frente a herpes zóster. Ponencia de Programa y Registro de Vacunaciones. Comisión de Salud Pública del CI-SNS, Ministerio de Sanidad, 25 marzo 2021

Importantes avances en vacunación frente a la malaria

2022, 97, 61–80

World Health Organization

Organisation mondiale de la Santé

Contents

61 Malaria vaccine: WHO position paper – March 2022

Malaria vaccine: WHO position paper – March 2022

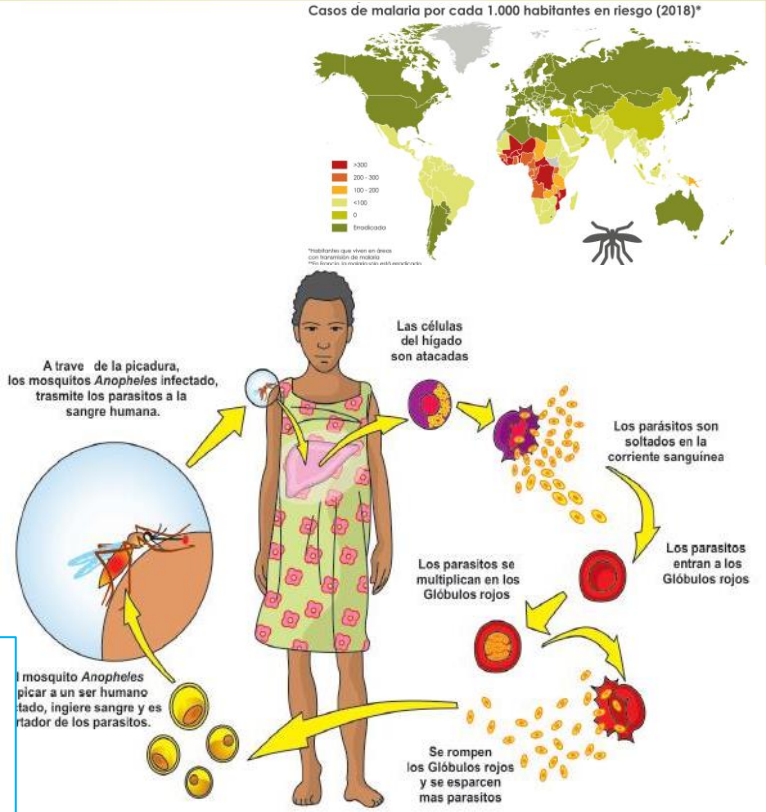
La OMS recomienda por primera vez en la historia una vacuna contra la malaria

La inmunización RTS,S (Mosquirix) es segura y tiene una eficacia que ronda el 40%, por lo que ha sido aprobada para su utilización a gran escala como método complementario de prevención. El paludismo causa alrededor de 400.000 muertes anuales, la mayoría de niños africanos menores de cinco años

Importantes avances en vacunación frente a la malaria

of the *World malaria report*.[3] According to the latest report, there were an estimated 241 million cases and 627 000 deaths globally in 2020.[3] Malaria is preventable and treatable. The global priority is to reduce the

largely in South-East Asia and South America.[3] Almost all malaria deaths are caused by *Plasmodium falciparum* and most occur in African children under 5 years of age. Adults who have lived in areas with high



- **1ª causa de mortalidad y enfermedad infantil en África**
- Malaria en embarazadas: 50% mortalidad (fetal o maternal).
- Adultos desarrollan inmunidad adquirida.

World malaria report 2021. Geneva: World Health Organization; 2021
OMS. WEEKLY EPIDEMIOLOGICAL RECORD, NO 9, 4 MARCH 2022

Primera vacuna frente a la malaria

Strong recommendation for , High certainty evidence

WHO Guidelines for malaria, 3 June 2022. Geneva: World Health Organization; 2022

Malaria vaccine (2021)

The RTS,S/AS01 malaria vaccine should be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission as defined by WHO.

- **Vacuna RTS,S/AS01 (Mosquirix®)**: Prevención de paludismo por *P. falciparum* **en niños desde 5 meses** de zonas de alta transmisión en África.
- Proteína recombinante que fusiona **antígeno RTS** de superficie de esporozoito de *P. falciparum* con **HBSAg**, adyuvado por AS01.
- Pauta: **4 dosis** (meses: 0, 1, 2 y 20)
- **Niños 5-17 meses**: eficacia vacunal **48 meses**: **39%** para malaria no complicada y **29%** para malaria severa; eficacia vacunal **14 meses**: **51%** para malaria no complicada y **45%** para malaria severa. [Eficacia vacunal 7 años: 37% frente malaria grave].
- **No eficaz en niños de <3 meses**.

Lancet. 2015 July 04; 386(9988): 31–45. doi:10.1016/S0140-6736(15)60721-8

setting. Among the older children, in the 12 months following administration of the first 3 doses, vaccine efficacy against clinical malaria (uncomplicated and severe) was 51% (95% CI 47–55) and against severe malaria was 45% (95% CI 22–60). Over a median of 46 months' follow-up after the third dose, in children who received a fourth dose 18 months after the third dose, vaccine efficacy against clinical malaria was 39% (95% CI 34–43) and against severe malaria 29% (95% CI 6–46) (per protocol analyses).[9] Over the same period,

Primera vacuna frente a la malaria

The NEW ENGLAND JOURNAL of MEDICINE

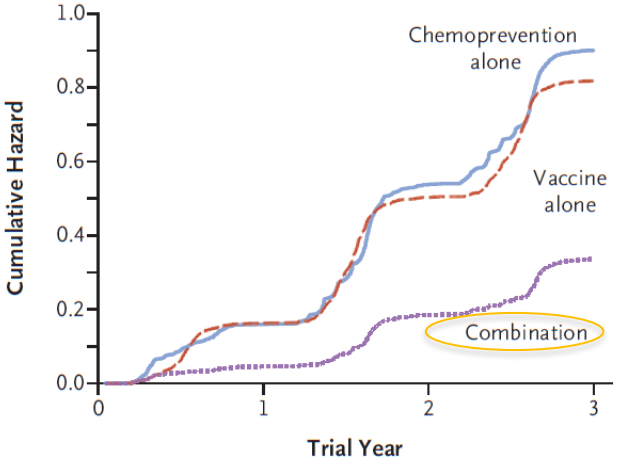
ORIGINAL ARTICLE

Seasonal Malaria Vaccination with or without Seasonal Malaria Chemoprevention

D. Chandramohan, I. Zongo, I. Sagara, M. Cairns, R.-S. Yerbanga, M. Diarra, F. Nikièma, A. Tapily, F. Sompougdou, D. Issiaka, C. Zoungrana, K. Sanogo,

- **Mosquirix®** en áreas con malaria estacional: pauta vacunal **estacional** (antes de estación lluviosa) **+ recuerdos anuales** (en estudio).
- **Combinado con quimioprofilaxis estacional**, eficacia vacunal del **63%** para malaria no complicada y **70%** para malaria severa/muerte.

Nelson–Aalen Cumulative Hazard Estimates



No. at Risk			
Chemoprevention alone	1904	1847	1716
Vaccine alone	1927	1882	1734
Combination	1919	1873	1740

N Engl J Med 2021;385:1005-17. DOI: 10.1056/NEJMoa2026330

Resultados prometedores frente a la malaria…

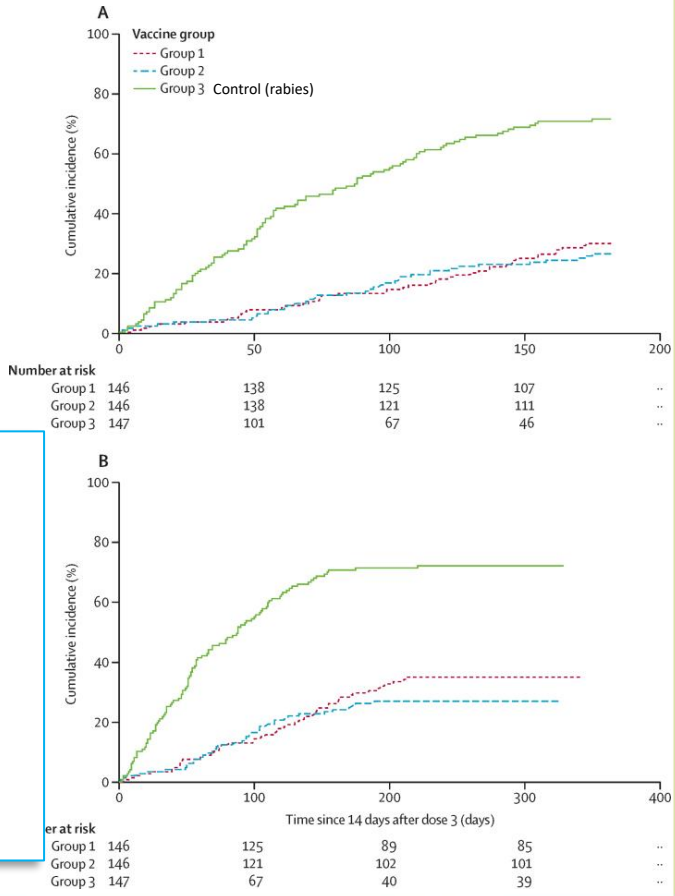
THE LANCET

ARTICLES | VOLUME 397, ISSUE 10287, P1809-1818, MAY 15, 2021

Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial

Mehreen S Datoo, MRCP * • Magloire H Natama, PhD * • Athanase Somé, MD • Ousmane Traoré, PhD •

- **Vacuna R21/Matrix-M**: prevención de paludismo por *P. falciparum* en niños de 5-17 meses de zonas de alta transmisión en África.
- Proteína recombinante que fusiona **proteína NF54** de esporozoito de *Plasmodium falciparum* con **HBSAg**, adyuvado por Matrix-M.
- Pauta: **3 dosis, antes de la estación lluviosa**.
- Población con 89% uso de mosquiteras y 93% quimioprofilaxis estacional.
- **Eficacia vacunal 6 meses:74-77%** para malaria no complicada.



Datoo et al. Lancet. 2021 May 15; 397(10287): 1809–1818.doi: 10.1016/S0140-6736(21)00943-0

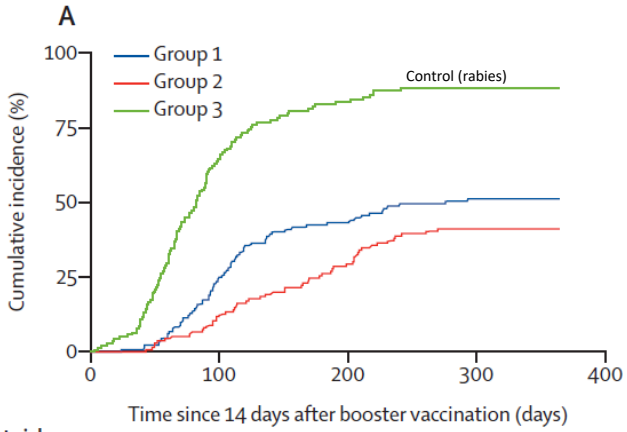
THE LANCET
Infectious Diseases

ARTICLES | ONLINE FIRST

Efficacy and immunogenicity of R21/Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase 1/2b randomised controlled trial

Mehreen S Datoo, MRCP * • Hamtandi Magloire Natama, PhD * • Athanase Somé, MD † •
Duncan Bellamy, MSc † • Ousmane Traoré, PhD • Toussaint Rouamba, PhD • et al. Show all authors •

- Pauta: 3 dosis **+ recuerdo al año** (antes de estación lluviosa).
- **Eficacia vacunal 24 meses: 71-80%** para malaria no complicada (en contexto de uso de mosquiteras y quimioprofilaxis estacional).



Number at risk

Group 1	132	100	72	59	..
Group 2	136	119	90	75	..
Group 3	140	49	21	25	..

Figure 2: Kaplan–Meier estimates of the time to first episode of clinical malaria according to the primary case definition

received the rabies vaccine developed clinical malaria by 12 months. Vaccine efficacy was 71% (95% CI 60 to 78) in the low-dose adjuvant group and 80% (72 to 85) in the high-dose adjuvant group. In the high-dose adjuvant group, vaccine efficacy against multiple episodes of malaria was 78% (95% CI 71 to 83), and 2285 (95% CI 1911 to 2568) cases of malaria were averted per 1000 child-years at risk among vaccinated children in the second year of follow-up. Among

Datoo et al. Lancet Infect Dis Sep 7,2022. DOI:10.1016/S1473-3099(22)00442-X

@Farmacia_LaPaz
@67CongresoSEFH

Gracias por su atención

Gràcies per la seva atenció

Eskerrik asko zure arretagatik

Grazas pola súa atención

REENCUENTRO REDEFINIR REFORMÚLATE RENACER