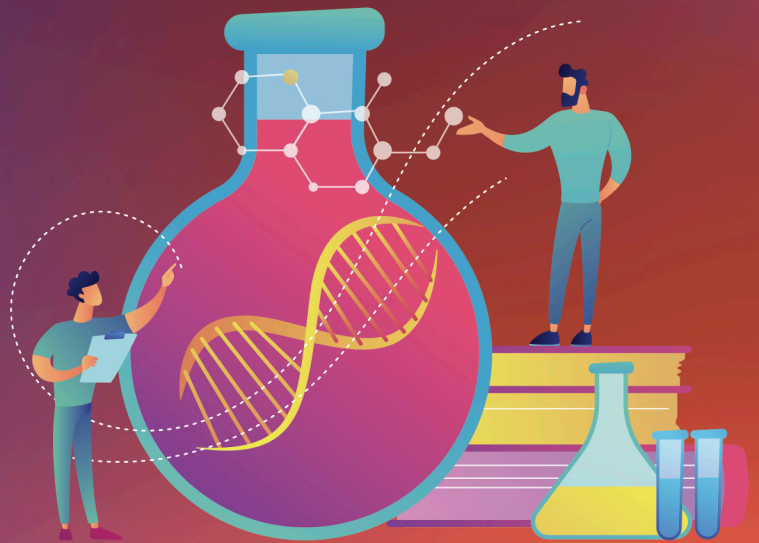
MEETING

GENOTIPADO DEL GEN UGT1A Y SU RELEVANCIA CLÍNICA

ORGANIZA

sefh
Sociedad Española
de Farmacia Hospitalaria

fefh
Fundación Española
de Farmacia Hospitalaria



MEETING

GENOTIPADO DEL GEN UGT1A Y SU RELEVANCIA CLÍNICA

MARTES, 10 DE NOVIEMBRE, 2020

17:00 - 18:10 h.

Save the Date!

Coordina: **Fernando Gutiérrez Nicolás**
Director Investigación Aplicada de la SEFH

Modera: **Marta Miarons Font**
Farmacéutica Especialista. Hospital Universitari Vall d'Hebron, Barcelona.

17:10-17.25
RELEVANCIA DE UGT1 EN CÁNCER COLORRECTAL
Pau Riera Armengol
Farmacéutico Especialista. Hospital de la Santa Creu i Sant Pau, Barcelona.

17:25-17.35
RELEVANCIA DE UGT1 EN CÁNCER DE PÁNCREAS
Lorenzo Cantarelli Grossi
Residente en Farmacia Hospitalaria. Hospital Universitario Ntra. Sra. de Candelaria, Sta. Cruz de Tenerife.

17:35-17.45
RELEVANCIA DE UGT1 EN LMC
Karen Ilenia Álvarez Tosco
Residente en Farmacia Hospitalaria. Hospital Universitario Ntra. Sra. de Candelaria, Sta. Cruz de Tenerife.

17:45-18:00
DEBATE

La jornada ha sido diseñada de tal forma que la Dra. Miarons realizará una introducción sobre la importancia que tiene el genotipado del gen UGT1A1 y como condiciona la farmacodinamia de diversos fármacos.
Posteriormente se expondrá la relevancia de este genotipado en diferentes patologías así como los ajustes farmacoterapéuticos pertinentes. Como viene siendo habitual, la jornada se cerrará con una debate abierto de los asistentes sobre el tema.

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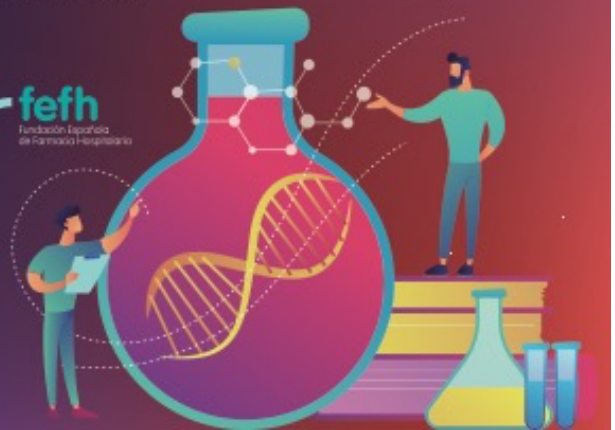
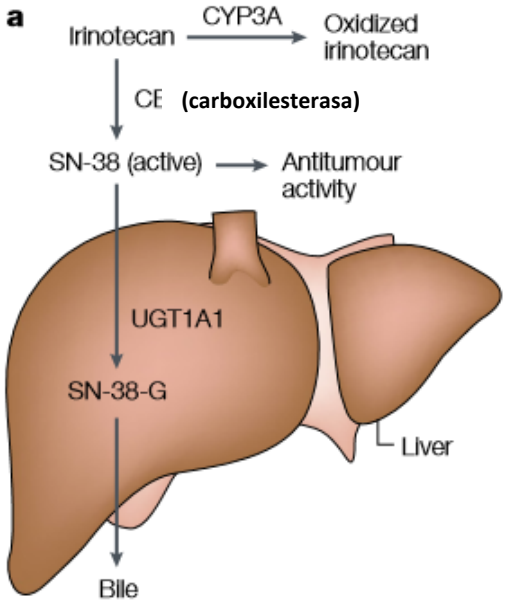
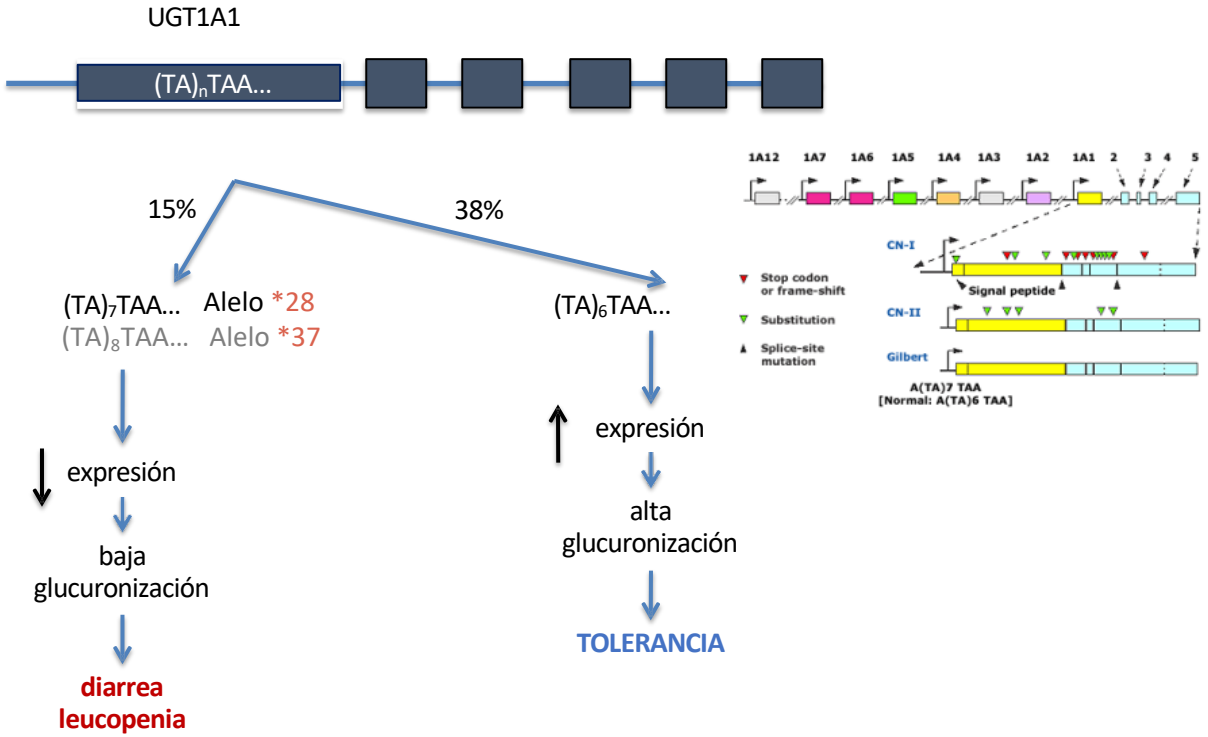
¡Regístrate a la sesión online!



POLIMORFISMOS QUE AFECTAN A LA FARMACODINAMIA DE IRINOTECAN





Relling M, Dervieux T. Nature Reviews Cancer. 2001;1:99-108.

APLICABILIDAD DE LA DETERMINACIÓN DEL POLIMORFISMO DE LA UGT1A1

1 Cáncer colorrectal

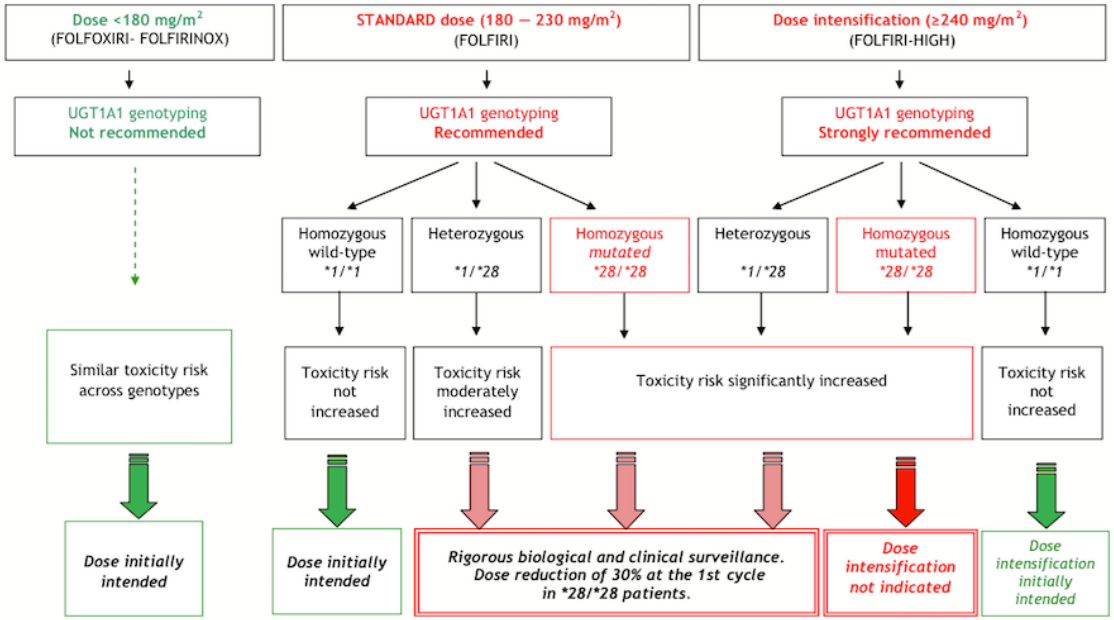
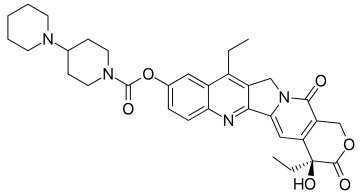


Figure 1 Decision tree for UGT1A1 genotyping depending on initially intended irinotecan dose.

Etienne-Grimaldi MC. Fundam Clin Pharmacol. 2015 Jun;29(3):219-37



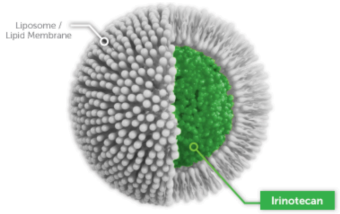
IRINOTECAN

PHENOTYPE (GENOTYPE)	THERAPEUTIC DOSE RECOMMENDATION	LEVEL OF EVIDENCE	CLINICAL RELEVANCE
*1/*28	None.	Published controlled studies of moderate quality* relating to phenotyped and/or genotyped patients or healthy volunteers, and having relevant pharmacokinetic or clinical endpoints..	Clinical effect (S): death; arrhythmia; unanticipated myelosuppression.
*28/*28	Dose >250mg/m²: reduce initial dose by 30%. Increase dose in response to neutrophil count. Dose <=250mg/m²: no dose adjustment.	Published controlled studies of moderate quality* relating to phenotyped and/or genotyped patients or healthy volunteers, and having relevant pharmacokinetic or clinical endpoints.	Clinical effect (S): Failure of lifesaving therapy e.g. anticipated myelosuppression; prevention of breast cancer relapse; arrhythmia; neutropenia < $0.5x10^9$/l; leucopenia < $1.0x10^9$/l; thrombocytopenia < $25x10^9$/l; life-threatening complications from diarrhea.

PharmGKB

APLICABILIDAD DE LA DETERMINACIÓN DEL POLIMORFISMO DE LA UGT1A1

2 Cáncer de páncreas



IRINOTECAN LIPOSOMAL

En los pacientes homocigóticos para el alelo UGT1A1*28, se debe valorar la posibilidad de comenzar con una dosis de inicio de ONIVYDE liposomal pegilado (irinotecán) reducida de 50 mg/m^2 (ver las secciones 4.8 y 5.1). Si se tolera en los ciclos siguientes, se debe considerar aumentar la dosis de ONIVYDE liposomal pegilado a 70 mg/m^2.

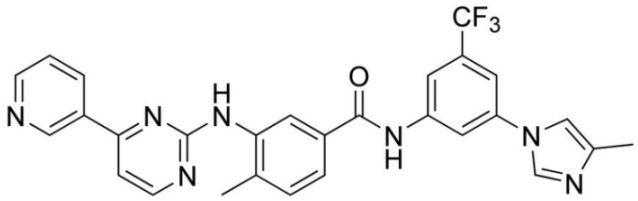
Procedures

All patients underwent *UGT1A1* genotype testing. Patients assigned nanoliposomal irinotecan plus fluorouracil and folinic acid (combination therapy arm) received an intravenous infusion of nanoliposomal irinotecan over 90 min at a dose of 80 mg/m² (equivalent to 70 mg/m² of irinotecan free base), followed by folinic acid 400 mg/m² over 30 min, then fluorouracil 2400 mg/m² over 46 h, every 2 weeks. For those allocated to the monotherapy arm, nanoliposomal irinotecan was administered at a dose of 120 mg/m² (equivalent to 100 mg/m² of irinotecan free base), every 3 weeks.[24,26] We reduced the initial nanoliposomal irinotecan dose for patients homozygous for the *UGT1A1*28* allele by 20 mg/m² then increased it to the standard dose after the first cycle in the absence of drug-related toxic effects.[27] Patients who were assigned fluorouracil and folinic acid (control arm) received 200 mg/m² of folinic acid as a 30-min infusion followed by an infusion of 2000 mg/m² fluorouracil over 24 h, every week for the

Wang-Gillam A, et al. Lancet. 2016;387(10018):545-557.

APLICABILIDAD DE LA DETERMINACIÓN DEL POLIMORFISMO DE LA UGT1A1

3 Leucemia mieloide crónica (LMC)



NILOTINIB

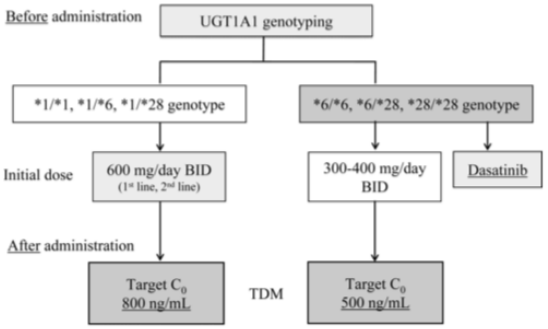


Fig. 4. A Proposed Therapeutic Strategy Using Nilotinib TDM for CML Patients

UGT1A1 promoter polymorphism increases risk of nilotinib-induced hyperbilirubinemia

J. B. Singer, Y. Shou, +8 authors O. Ottmann · Published 2007 · Medicine, Biology · Leukemia

Influence of *UGT1A1* *6, *27, and *28 Polymorphisms on Nilotinib-induced Hyperbilirubinemia in Japanese Patients with Chronic Myeloid Leukemia

Maiko ABUMIYA, Naoto TAKAHASHI, Takenori NIIOKA, Yoshihiro KAMEOKA, Naohito FUJISHIMA, Hiroyuki TAGAWA, Kenichi SAWADA, Masatomo MIURA

Reducir dosis a 300-400 mg/día

Masamoto M. Biol Pharm Bull. 2015;38:645–654.

APLICABILIDAD DE LA DETERMINACIÓN DEL POLIMORFISMO DE LA UGT1A1